UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,545	12/17/2003	Masahiro Kawaguchi	03500.017338	6817

5514 7590 12/21/2005

FITZPATRICK CELLA HARPER & SCINTO
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
LIU, SUE XU	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/736,545	KAWAGUCHI ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *1 and 8-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/10/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II (Claims 2-7) in the reply filed on 11/14/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election **without traverse** (MPEP § 818.03(a)).

2. Applicant's non-election of Claims 1 and 8-26 in the reply filed on 11/14/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election **without traverse** (MPEP § 818.03(a)).

3. Claims 1 and 8-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/14/2005.

4. Applicants also elected the following species:

A.) fluorescent markers;

B.) two kinds of external standard probes;

C.) one kind of internal standard probes;

D.) single-stranded DNA;

E.) 20 residues each of internal and external probes;

F.) two sets of primers that will produce 500 bp and 200 bp products;

G.) a "microorganism'" is selected as the most specific species explicitly recited in the specification;

H.) one nucleic acid;

I.) two.

Accordingly, the non-elected species are withdrawn from each corresponding claims.

5. Claims 1-22 are currently pending;

Claims 8 and 12-22 have been withdrawn;

Claims 1-7 and 9-11 are being examined in this application.

Priority

6. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on 6/28/2002. It is noted, however, that applicant has not filed a certified copy of the JAPAN 2002-191390 application as required by 35 U.S.C. 119(b).

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on 6/24/2002. It is noted, however, that applicant has not filed a certified copy of the JAPAN 2002-183249 application as required by 35 U.S.C. 119(b).

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on 6/23/2003. It is noted, however, that applicant has not filed a certified copy of the PCT/JP03/07918 application as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 112

7. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

8. Claims 2-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims briefly recite a DNA micro-array for detecting nucleic acid molecules comprising probes for target samples, internal control probes and external control probes. The internal probes hybridize to internal standard nucleic acids with the intended use for "quantitative evaluation of PCR...", and the external probes hybridize to external standard nucleic acids with the intended use for "evaluation of accuracy of detection...". The specification of the instant application discloses the internal standard probe as "a probe for detecting an internal standard nucleic acid to be used to assist quantitative determination of a target nucleic acid," and the internal standard nucleic acid as "a nucleic acid of a known base sequence" (page 12 of the specification). The external standard nucleic is also disclosed as "a nucleic acid having a known base sequence to be added to a sample..." and "has no base sequence homology to the base sequence of the target nucleic acid." Therefore, the internal and

the external standards and probes could be any nucleic acid sequences that are known, and are not the target sequences.

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

Written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not case involves question of priority, since requirement applies to all inventions including chemical inventions, and since the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide description of compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993)

(bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

Although the instant specification recites examples of DNA microarrays comprising certain specific probes (including target, internal and external probes), the instant specification and/or the aforementioned claims do not provide adequate written description to show possession of the entire genus of microarrays that comprise various probes. More specifically, the specification and/or the claims do not adequately describe the entire genus of probes including "internal" and "external" probes. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The instant claims and/or specification only vaguely described the internal and external probes to be known nucleic acid sequences that would not hybridize to target sequences. No specific structurally and functional information regarding the probes were described. The instant

specification only provided examples of a few probe sequences, but recited no specific structural and/or functional descriptions for the entire genus of probes. Each species within each genus of internal or external probes could have different structure and/or function from each other.

As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of "target probes", "internal probes", and "external probes" as well as internal and external standards, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of creating such composition. Adequate written description requires more than a mere statement that it is part of the invention and reference to a possibility of creating it. The composition itself is required.

Therefore, the instant Claims 2-7 do not meet the written description provision of 35 U.S.C. 112, first paragraph.

9. The following is a quotation of the **second paragraph of 35 U.S.C. 112**:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 2-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims recite the phrase "substantially complementary to the target sequences" (Claim 1), which is indefinite since it does not provide any distinct structural or functional limitation on the nucleic acid probes. The claim could read on probes having 50-100% complementarity to the target sequences. Probes that are 50% complement to the target could be structurally and functionally different from the ones that are 100% different. It is not

clear from either the instant specification or the claims which probes are claimed for the invention.

The instant claims also recite probes for both "internal" and "external" standards, which are not distinctly defined in either the specification or the claims. The only limitation provided for both of the internal and external probes are that they are known sequences that are different from the target sequence. These do not provide distinct structural and/or functional limitation on the probes, which could be any sequence. A person skilled in the art would not be able to determine the metes and bounds of the invention. That is a skilled artisan would not be able to determine what sequences are included as the probes.

The instant claims recite "at least four levels of amount or density" (in Claim 3), which does not distinctly define the structure of the microarray. The phrase "at least" is not definite and could read on various ranges of "amount or density".

The instant claims recite "two probes corresponding to PCR products", which does not provide distinct structural and/or functional limitations for the "probes". The phrase "corresponding to" is not defined in either the instant specification or the claims, and could be interpreted to mean "complementary to" or "related to", for examples. Without specifically provide a definition such as percentage of complementarity, a person skilled in the art would not be able to determine the structural and/or functional limitation of the claimed probes on the microarray.

The instant claims recite "two probes each having a mutually different base sequence of any length" (in Claim 5). The phrase "mutually different base sequence" does not distinctly and

clearly define the probe sequences, and the phrase "any length" also does not prove distinct structural limitation on the probe.

Therefore, as described above, the instant claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 2-7 are rejected under 35 U.S.C. **102(b)** as being anticipated by Dudley et al (PNAS. Vol. 99: 7554-7559. May 28, 2002).

The instant claims briefly recite a DNA micro-array for detecting nucleic acid molecules comprising probes for target samples, internal control probes and external control probes. The internal probes hybridize to internal standard nucleic acids with the intended use for "quantitative evaluation of PCR...", and the external probes hybridize to external standard nucleic acids with the intended use for "evaluation of accuracy of detection...". The specification of the instant application discloses the internal standard probe as "a probe for detecting an internal standard nucleic acid to be used to assist quantitative determination of a target nucleic acid," and the internal standard nucleic acid as "a nucleic acid of a known base sequence" (page 12 of the specification). The external strandard nucleic is also discloesed as "a nucleic acid having a known base sequence to be added to a sample..." and "has no base sequence homology to the base sequence of the target nucleic acid." Therefore, the internal and

the external standards and probes could be any nucleic acid sequences that are known, and are not complementary to the target sequences.

Dudley et al teach measuring absolute expression with microarrays with a calibrated reference sample, and generating ratios between sample intensities and intensities of the oligo reference measure sample RNA levels (See Abstract of the reference). The reference teaches microarrays comprising probes generated from yeast ORF PCR product set, and an oligo reference sample with certain nucleic acid sequence (See page 7554, right column, 4th paragraph of the reference). The yeast ORF PCR product set contains over 6,000 yeast ORF (see the Supplementary Web Site described on Page 7555, left column, last paragraph of the reference), which could contain the "target nucleic acid" (could be any yeast gene of interest from the >6,000 ORF PCR products). The oligo reference sample could be either the "internal" or "external" probes for the internal or external standards since the oligo sequence is known and contained on the microarray. In addition, any other probes for the >6,000 genes that is not the considered to be the gene of interest (the target gene) and is not complementary to the target gene sequence could be considered as either the internal or the external probes. For example, the RPL29, or the PHO88 genes listed in Figure 3 on Page 7557. The probes for these genes on the microarray would hybridize to genes with different PCR products (different lengths). The reference further teaches that the microarray are generated either by printing PCR generated cDNA or commercially available oligo sets (See Supplemental Web Site as described on Page 7555, left column, last paragraph of the reference), which would refer to synthetic nucleic acids immobilized on the substrate. In addition, the reference teaches the oligo reference sample is 20 bases long (page 7554, right column, 4th paragraph of the reference), which would refer to

nucleic acid has a chain length of 15 to 75 bases. The reference further teaches the Yeast Genome Oligo Set were printed at a concentration of 10 pmols/ml in 150 mM potassium phosphate (See Supplemental Web Site as described on Page 7555, left column, last paragraph of the reference), which would refer to the probes are immobilized on the substrate as a group of at least four levels of amount of density.

Thus, the reference clearly anticipates the claimed invention.

12. Claims 2 and 4-7 are rejected under 35 U.S.C. **102(b)** as being anticipated by Delenstarr et al (US PGPUB 2002/0051973 A1; May 2, 2002).

The instant claims briefly recite a DNA micro-array for detecting nucleic acid molecules comprising probes for target samples, internal control probes and external control probes. The internal probes hybridize to internal standard nucleic acids with the intended use for "quantitative evaluation of PCR...", and the external probes hybridize to external standard nucleic acids with the intended use for "evaluation of accuracy of detection...". The specification of the instant application discloses the internal standard probe as "a probe for detecting an internal standard nucleic acid to be used to assist quantitative determination of a target nucleic acid," and the internal standard nucleic acid as "a nucleic acid of a known base sequence" (page 12 of the specification). The external standard nucleic is also disclosed as "a nucleic acid having a known base sequence to be added to a sample..." and "has no base sequence homology to the base sequence of the target nucleic acid." Therefore, the internal and the external standards and probes could be any nucleic acid sequences that are known, and are not complementary to the target sequences.

Delenstarr et al teach a set of features comprising oligophophodiester probes (would refer to microarrays; Claim 1 of the reference). The reference teaches hybridization features comprising hybridization probes (bound to a surface; Claim 2 of the reference) that selectively hybridize to a detectably labeled target nucleotide sequence (would refer to the probes for the target nucleic acid; Claim 1 of the reference). The reference also teaches background features comprising background probes (as listed in Claim 4 of the reference) that do not selectively hybridize to said nucleotide sequence (would refer to either the internal and/or external probes; Claims 2 and 4 of the reference). In addition, the reference teaches the features (or array) comprising target probes, test-background probes (would refer to either internal or external probes), and standard-background probes (would refer to either internal or external probes); (See Claim 30 of the reference). The reference also teaches the probes could be 25 bases long (such as SEQ ID NO 5 as recited in Claim 5, for example). Furthermore, the reference recites various different probes with different sequences (such as the one directed in Claim 5 of the reference), which have the functions of hybridizing to PCR products with different chain lengths. The reference further teaches that the probes can be synthesized (See paragraph [0104] of the reference).

Thus, the reference clearly anticipates the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL
Art Unit 1639
12/05/2005

PADMASHRI PONNALURI
PRIMARY EXAMINER